

21. (Twice Amended) A method for the differential diagnosis of ischemic and hemorrhagic cerebral events comprising:
- analyzing a body fluid of a patient to detect presence and concentration level of one or more ischemic marker proteins selected from the group consisting of myelin basic protein (MBP), the beta isoform of S100 protein (S100), and neuronal specific enolase (NSE); said analyzing comprising contacting said one or more ischemic marker proteins with a reagent capable of detecting said marker proteins, and removing reagent that does not detect said marker proteins,
  - analyzing a body fluid of said patient to detect presence and concentration level of a brain endothelial cell membrane protein, said analyzing comprising contacting said brain endothelial cell membrane protein with a reagent capable of detecting said endothelial cell membrane protein, and removing reagent that does not detect said brain endothelial cell membrane protein,
  - comparing the concentration level of each protein detected in steps (a) and (b) to specific threshold values to determine the presence of statistically significant concentrations thereof,
  - assessing patient condition by comparing said presence or absence of statistically significant concentrations of said protein; in accordance with an analytical flowchart; and
  - determining whether the patient condition assessed in step (d) is an ischemic cerebral event or an hemorrhagic cerebral event.
23. (Twice Amended) A method as defined in claim 21 wherein said body fluid is selected from the group consisting of blood, a blood product and cerebrospinal fluid.
24. (Twice Amended) A method as defined in claim 21 wherein said brain endothelial cell membrane protein is selected from one or more of the group consisting of Thrombomodulin, Glucose Transporter I in the dimeric or tetrameric form, Neurothelin, Gamma Glutamyl Transpeptidase, and P-glycoprotein.

26. (Twice Amended) A method as defined in claim 21 further comprising:  
analyzing said body fluid to detect presence and concentration level of a secondary marker protein, said secondary marker protein being from the cell type of one of said myelin basic protein, beta isoform of S100 protein or neuronal specific enolase, whereby the time of onset of a hemorrhagic or ischemic cerebral event can be determined.
34. ~~(Amended) The method in accordance with claim 21, wherein in step e, if MBP, S100, NSE and brain endothelial cell membrane proteins are assessed in step a and b, and only said NSE is elevated, then said patient condition is an ischemic cerebral event; or wherein in step e, if MBP, S100, NSE and brain endothelial cell membrane protein are assessed in step a and b, and only said brain endothelial cell membrane protein is elevated, then said patient condition is an ischemic cerebral event; or wherein in step e, if S100 is present then said patient condition is an ischemic cerebral event; or wherein in step e, if NSE along with any of MBP, S100 or a brain endothelial cell membrane protein are present, then said patient condition is an ischemic cerebral event, or wherein in step e, if brain endothelial cell membrane protein, with any of MBP, NSE, or S100 are present, then said patient condition is an ischemic cerebral event; or wherein in step e, if S100 is present with elevated NSE and normal levels of brain endothelial cell membrane protein, then said patient condition is an ischemic cerebral event; or wherein in step e, if S100 is present alone, or along with elevated NSE or Tm, then said patient condition is an ischemic cerebral event; or wherein in step e, if MBP is present at a level 200 times normal or greater, then said patient condition is a hemorrhagic cerebral event; or wherein in step e, if S100 and NSE levels are elevated, and MBP and Tm levels are normal, then said patient condition is a hemorrhagic cerebral event; or wherein in step e, if S100 and MBP are elevated, then said patient condition is a hemorrhagic cerebral event.~~
40. (Amended) A method for determining that brain injury has occurred comprising:  
(a) analyzing a body fluid of a patient to detect presence and concentration level of two or more proteins selected from the group consisting of myelin basic protein (MBP), the beta isoform of S100 protein (S100), neuronal specific enolase (NSE) and a brain endothelial cell membrane protein;

- (b) comparing the concentration level of each protein detected in step a to specific threshold values to determine the presence of a statistically significant concentration thereof; and
  - (c) determining if two or more of said proteins are present in a statistically significant concentration, wherein the presence of two or more of said proteins in a statistically significant concentration is indicative that an injury to the brain has occurred.
41. (Amended) A method for diagnosing an ischemic or hemorrhagic cerebral event comprising:
- (a) analyzing a body fluid of a patient to detect the presence and concentration level of four proteins comprising myelin basic protein (MBP), the beta isoform of S100 protein (S100), neuronal specific enolase (NSE) and a brain endothelial cell membrane protein;
  - (b) comparing the concentration level of each said protein detected in step a to specific threshold values to determine the presence of a statistically significant concentration thereof;
  - (c) assessing patient condition by comparing said presence or absence of statistically significant concentrations of said proteins in accordance with an analytical flow chart; and
  - (d) determining whether the patient condition assessed in step c is an ischemic cerebral event or an hemorrhagic cerebral event.
45. (Amended) The method of Claim 44, wherein said first sample and said second sample of body fluid are taken at different times.
46. (Amended) The method of Claim 41 wherein step (c) comprises determining if said one or more of said proteins are present at a statistically significant concentration wherein the presence of one or more of said proteins is indicative that injury to the brain has occurred.

47. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of only NSE at a statistically significant concentration is indicative that said brain injury is a transitory ischemic attack (TIA).
48. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of NSE and one or more proteins selected from the group consisting of MBP, S100, and a brain endothelial cell membrane protein at a statistically significant concentration is indicative that said brain injury is a cerebral infarction.
49. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of only a brain endothelial cell membrane protein at a statistically significant concentration is indicative that said brain injury is a lunar infarction.
50. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of a brain endothelial cell membrane protein and one or more proteins selected from the group consisting of MBP, S100, and NSE at statistically significant concentrations is indicative that said brain injury is a cerebral infarction.
51. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of MBP at a concentration of greater than about 200 times the normal level is indicative that said brain injury is an intracerebral hemorrhage.
52. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of S100 at a statistically significant concentration is indicative that said brain injury is a cerebral infarction or a subarachnoid hemorrhage.
53. (Amended) The method of Claim 41 further comprising assessing the type of brain injury wherein the presence of S100 and NSE at a statistically significant concentration and the absence of any other markers is indicative that said brain injury is a subarachnoid hemorrhage.

Add new Claims 54-59 as follows.

54. (New) The method of Claim 34, wherein if MBP, S100, NSE and brain endothelial cell membrane protein are assessed, and only NSE is present, then said ischemic cerebral event is a transitory ischemic attack.
55. (New) The method of Claim 34, wherein if MBP, S100, NSE and brain endothelial cell membrane protein are assessed, and only a brain endothelial cell membrane protein is present, then said ischemic cerebral event is a lacunar infarct.
56. (New) The method of Claim 34, wherein if S100 is present or if NSE along with any of MBP, S100 or a brain endothelial cell membrane protein are present, or if brain endothelial cell membrane protein, with any one of MBP, NSE, or S100, or if S100 is present with elevated NSE and normal levels of a brain endothelial cell membrane protein, then said ischemic cerebral event is an evolving cerebral infarct.
57. (New) The method of Claim 34, wherein if MBP is present at a level about 200 times normal or greater, then said hemorrhagic cerebral event is an intracerebral edema.
58. (New) The method of Claim 34, wherein if S100 and NSE are elevated, and MBP and brain endothelial cell membrane protein levels are normal, then said hemorrhagic cerebral event is a subarachnoid hemorrhage.
59. (New) The method of Claim 34, wherein if S100 and MBP are elevated, then said hemorrhagic cerebral event is a cerebral edema.

### REMARKS

#### Amendments to the Claims

Support for the amendment of Claim 21 can be found throughout the specification, for example, at pages 13 to 27. Support for the amendment of Claim 26 can be found throughout the specification, for example, at page 9, line 21 to page 11, line 1. Support for the amendment of Claim 34 can be found throughout the specification, for example, at pages 15 to 27 and FIG. 2. Support for the amendment of Claim 40 can be found throughout the specification, for example,